

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>			Docket Number (Optional) CIBT-P03-031		Application Number 09/827,110			
APR 25 2002 RECEIVED JCS			Applicant Wang, Elizabeth					
			Filing Date April 5, 2001		Group Art Unit 1653			
U.S. PATENT DOCUMENTS								
EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE		
RT	AA	6,159,950	12/20/00	Crystal et al.				
	AB	5,844,079	12/1/98	Ingham et al.				
	AC	5,837,538	11/17/98	Scott et al.				
	AD	5,789,543	8/4/98	Ingham et al.				
	AE	5,759,811	6/2/98	Epstein et al.				
	AE	5,747,507	5/5/98	Ikegaki et al.				
	AG	5,643,915	7/1/97	Andrulis, Jr. et al.				
	AH	5,585,087	12/17/96	Lustig et al.				
	AI	5,519,035	5/21/96	Maiese et al.				
	AJ	5,223,408	6/29/93	Goeddel et al.				
	AK	4,456,687	6/26/84	Green				
FOREIGN PATENT DOCUMENTS								
	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation		
						YES	NO	
RT	AL	DE 39 42 114 A1	12/20/89	GERMANY				
	AM	EP 0879888 A2	11/25/98	Europe				
	AN	EP 0874048 A2	10/28/98	Europe				
	AO	EP 0249873 A2	6/10/87	Europe				
	AP	EP 0187371 A2	7/16/86	Europe				
	AQ	JP 63088112		Japan				
	AR	JP 04305528		Japan				
	AS	JP 02273610		Japan				
	AT	WO 99/10004	3/4/99	PCT				
	AU	WO 99/04775	2/4/99	PCT				
	AV	WO 99/01468	1/14/99	PCT				
	AW	WO 99/00403	1/7/99	PCT				
	AX	WO 99/00117	1/7/99	PCT				
	AY	WO 98/35020	8/13/98	PCT				

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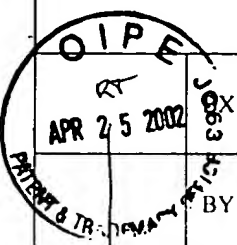
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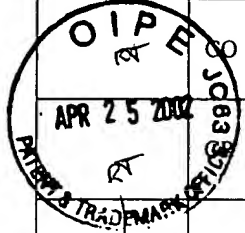
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BD	WO 98/12326	3/26/98	PCT			
BE	WO 97/45541	12/4/97	PCT			
BF	WO 97/11095	3/27/97	PCT			
BG	WO 96/17924	6/13/96	PCT			
BH	WO 96/16668	6/6/96	PCT			
BI	WO 96/11260	4/18/96	PCT			
BJ	WO 96/09806	4/4/96	PCT			
BK	WO 95/23223	8/31/95	PCT			
BL	WO 95/18856	7/13/95	PCT			
BM	WO 94/28016	12/8/94	PCT			
BN	WO 92/15679	9/17/92	PCT			
BO	WO 90/02809	3/22/90	PCT			

OTHER DOCUMENTS


(Including Author, Title, Date, Pertinent Pages Etc.)

BP	Anderson, R. et al. Maintenance of ZPA signaling in cultured mouse limb bud cells. <i>Devel.</i> 117, 1421-1433 (1993).
BQ	Angler, N. Biologists find key genes that shape patterning of embryos. <i>N. Y. Times</i> C-1 (11 January 1994).
BR	Basler, K. & Struhl, G. Compartment boundaries and the control of Drosophila limb pattern by Hedgehog protein. <i>Nature</i> 368, 208-214 (1994).
BS	Bass, D. et al. Hormone phage: An enrichment method for variant proteins with altered binding properties. <i>PROTEINS: Structure, Function and Genetics</i> 8, 309-314 (1990).
BT	Bejsovec, A. & Wieschaus. Segment polarity gene interactions modulate epidermal patterning in Drosophila embryos. <i>Devel.</i> 119, 501-517 (1993).
BU	Bienz, M. Homeotic genes and positional signaling in the Drosophila viscera. <i>TIG</i> 10, 22-26 (January 1994).
BV	Bitgood, M. & McMahon, A. Hedgehog and Bmp genes are coexpressed at many diverse sites of cell-cell interaction in the mouse embryo. <i>Dev. Biol.</i> 172, 126-138 (1995).
BW	Blair, S. S. Hedgehog digs up an old friend. <i>Nature</i> 373, 656-657 (23 February 1995).

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		Brand-Saberi, B. et al. The ventralizing effect of the notochord on somite differentiation in chick embryos. <i>Anat. Embryol.</i> 188, 239-245 (1993).	
		Brookes, J. We may not have a morphogen. <i>Nature</i> 350, 15 (1991).	
	BZ	Bumcrot, D. A. & McMahon, A. Somite differentiation. Sonic signals somites. <i>Curr. Biol.</i> 5, 612-614 (June 1995).	
	CA	Bumcrot, D. A. & McMahon, A. Sonic hedgehog: Making the gradient. <i>Chem. Biol.</i> 3, 13-16 (January 1996).	
	CB	Bumcrot, D. A. et al. Proteolytic processing yields two secreted forms of sonic hedgehog. <i>Mol. Cell. Biol.</i> 15, 2294-2303 (April 1995).	
	CC	Charite, J. et al. Ectopic expression of Hoxb-8 causes duplication of the ZPA in the forelimb and homeotic transformation of axial structures. <i>Cell</i> 78, 589-601 (1994).	
	CD	Coffman et al. Xotch, the <i>Xenopus</i> homolog of <i>Drosophila</i> notch. <i>Science</i> 249, 1438-1441 (1990).	
	CE	Concordet, J. & Ingham, P. Developmental biology. Patterning goes sonic. <i>Nature</i> 375, 279-280 (May 1995).	
	CF	Curry et al. Sequence analysis reveals homology between two problems of the flagellar radial spoke. <i>Mol. Cell. Biol.</i> 12, 3967-3977 (1992).	
	CG	Davidson, E. H. How embryos work: a comparative view of diverse modes of cell fate specification. <i>Devel.</i> 108, 365-389 (1990).	
	CH	Davis, A. P. & Capecchi, M. R. Axial homeosis and appendicular skeleton defects in mice with a targeted disruption of <i>hoxd-1</i> . <i>Development</i> 120, 2187-2198 (1994).	
	CI	Dickinson, W. Molecules and morphology: Where's the homology? <i>TIG</i> 11, 119-120 (1995).	
	CJ	Dingemans, M. A. et al. The expression of liver-specific genes within rat embryonic hepatocytes is a discontinuous process. <i>Differentiation</i> 56, 153-162 (1994).	
	CK	Dolle, P. et al. Coordinate expression of the murine Hox-5 complex contacting genes during limb pattern formation. <i>Nature</i> 342, 767-772 (1989).	
	CL	Dolle, P. et al. Disruption of the Hoxd-13 gene induces localized heterochrony leading to mice with neonatal limbs. <i>Cell</i> 75, 431-441 (1993).	
CM	Echelard, Y. et al. Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity. <i>Cell</i> 75, 1417-1430 (1993).		
CN	Ekker, S. et al. Distinct expression and shared activities of members of the hedgehog gene family of <i>Xenopus laevis</i> . <i>Develop.</i> 121, 2337-2347 (August 1995).		

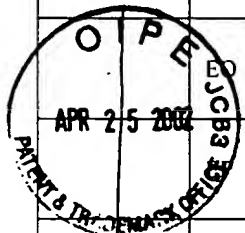
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		Ericson, J. et al. Sonic hedgehog induces the differentiation of ventral forebrain neurons: a common signal for ventral patterning within the neural tube. <i>Cell</i> 81, 747-756 (June 1995).	
		Ettelaie, C. et al. The effect of lipid peroxidation and lipolysis on the ability of lipoproteins to influence thromboplastin activity. <i>Biochem. Biophys. Acta.</i> 1257, 25-30 (June 1995).	
	CQ	Fahrner, K. et al. FGF-2: Apical ectodermal ridge growth in embryonic and adult mice. <i>EMBO J.</i> 6, 1265-1271 (1987).	
	CR	Fallon, J. F. et al. FGF-2: Apical ectodermal ridge growth signal for chick limb development. <i>Science</i> 264, 104-107 (1994).	
	CS	Fan, C. et al. Long-range sclerotome induction by sonic hedgehog: Direct role of the amino-terminal cleavage product and modulation by the cyclic AMP signaling pathway. <i>Cell</i> 81, 457-465 (5 May 1995).	
	CT	Fietz, M. et al. The hedgehog gene family in Drosophila and vertebrate development. <i>Devel. (Suppl.)</i> 43-51 (1994).	
	CU	Forbes, A. J. et al. Genetic analysis of hedgehog signaling in the Drosophila embryo. <i>Devel.</i> 119 (Suppl.), 115-124 (1993).	
	CV	Francis, P. H. et al. Bone morphogenetic proteins and a signaling pathway that controls patterning in the developing chick limb. <i>Devel.</i> 120, 209-218 (1994).	
	CW	Gallop, M. et al. Applications of combinatorial technologies to drug discovery. 1. Background and peptide combinatorial libraries. <i>J. Med. Chem.</i> 37, 1233-1251 (1994).	
	CX	Gerard, M. et al. Structure and activity of regulatory elements involved in the activation of the Hoxd-11 gene during late gastrulation. <i>EMBO J.</i> 12, 3539-3550 (1993).	
	CY	Gurdon, J. B. The generation of diversity and pattern in animal development. <i>Cell</i> 68, 185-199 (1992).	
	CZ	Gustin, K. et al. Characterization of the Role of Individual Protein Binding Motifs within the Hepatitis B Virus Enhancer I on X Promoter Activity Using Linker Scanning Mutagenesis. <i>Virology</i> 193, 653-660 (1993).	
	DA	Hall, T. et al. A potential catalytic site revealed by the 1.7-A crystal structure of the amino-terminal signaling domain of sonic hedgehog. <i>Nature</i> 378, 212-216 (November 1995).	
	DB	Halpern, et al. Induction of Muscle Pioneers and Floor Plate is Distinguished by the Zebrafish no Tail Mutation. <i>Cell</i> 75, 99-111 (8 October 1993).	
	DC	Hamburger, V. & Hamilton, H. L. A series of normal stages in the development of the chick embryo. <i>J. Morph.</i> 88, 49-92 (1951).	
DD	Matthias Hammerschmidt, et al., Protein Kinase A is a Common Negative Regulator of Hedgehog Signaling in the Vertebrate Embryo (1996) <i>Genes & Development</i> 10: 647-658		
DE	Hammerschmidt, M. et al. The world according to hedgehog. <i>TIG</i> 13 14-21 (1997).		

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PT	DF	Haramis, A. et al. The limb deformity mutation disrupts the SHH/FGF-4 feedback loop and regulation of 5' HoxD genes during limb pattern formation. <i>Devel.</i> 121, 4161-4170 (December 1995).	
RT		Hardy, A. et al. Gene expression, polarising activity and skeletal patterning in reaggregated hind limb mesenchyme. <i>Devel.</i> 121, 4329-4337 (December 1995).	
APR 25 2002	DH	C.S. Harmon, et al., Evidence that Activation of Protein Kinase A Inhibits Human Hair Follicle Growth and Hair Fibre Production in Organ Culture and DNA Synthesis in Human and Mouse Hair Follicle Organ Culture, (1997) British Journal of Dermatology 136: 853-858	
	DI	Hatta, K. et al. The cyclops mutation blocks specification of the floor plate of the zebrafish central nervous system. <i>Nature</i> 350, 339-341 (1991).	
	DJ	Heemskerk, J. & DiNardo, S. Drosophila hedgehog acts as a morphogen in cellular patterning. <i>Cell</i> 76, 449-460 (1994).	
	DK	Herberlein, U. et al. The TGBB homolog dpp and the segment polarity gene hedgehog are required for propagation of a morphogenetic wave in the Drosophila retina. <i>Cell</i> 75, 913-926 (1993).	
	DL	Hidalgo, A. & Ingham, P. Copatterning in the Drosophila segment: spatial regulation of the segment polarity gene patched. <i>Devel.</i> 110, 291-301 (1990).	
	DM	Hooper, J. & Scott, M. The Drosophila patched gene encodes a putative membrane protein required for segmental patterning. <i>Cell</i> 59, 751-765 (1989).	
	DN	Hynes, R. O. Induction of midbrain dopaminergic neurons by Sonic hedgehog. <i>Neuron</i> 15, 35-44 (July 1995).	
	DO	Hynes, R. O. Integrins: A family of cell surface receptors. <i>Cell</i> 48, 549-554 (1987).	
	DP	Ingham, P. W. Hedgehog points the way. <i>Current Biology</i> 4, 347-350 (1994).	
	DQ	Ingham, P. W. Localized hedgehog activity controls spatial limits of wingless transcription in the Drosophila embryo. <i>Nature</i> 366, 560-562 (1993).	
	DR	Ingham, P. W. Signaling by hedgehog family proteins in Drosophila and vertebrate development. <i>Curr. Opin. Genet. Dev.</i> 5, 478-484 (August 1995).	
	DS	Ingham, P. W. & Hidalgo, A. Regulation of wingless transcription in the Drosophila embryo. <i>Devel.</i> 117, 283-291 (1993).	
	DT	Ingham, P. W. et al. Role of the Drosophila patched gene in positional signaling. <i>Nature</i> 353, 184-187 (1991).	
	DU	Izpisua-Belmonte, J.-C. et al. Expression of Hox-4 genes in the chick wings links pattern formation to the epithelial-mesenchymal interaction that mediate growth. <i>EMBO J.</i> 11, 1451-1457 (1992).	
	DV	Izpisua-Belmonte, J.-C. et al. Expression of the homeobox Hox-4 genes and the specification of position in chick wing development. <i>Nature</i> 350, 585-589 (1991).	

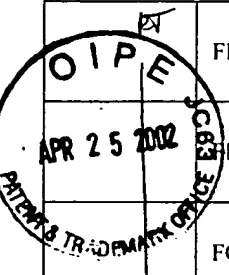
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	DW	Jiang, J. & Struhl, G. Protein kinase A in hedgehog signaling in Drosophila limb development. <i>Cell</i> 80, 563-572 (February 1995).	
		Jessel, T. M. & Melton, D. A. Diffusible factors in vertebrate embryonic induction. <i>Cell</i> 68, 257-270 (1992).	
	DY	Johnson, R. L. & Tabin, C. The long and short of hedgehog signaling. <i>Cell</i> 81, 313-315 (5 May 1995).	
	DZ	Johnson, R. L. et al. Ectopic expression of sonic hedgehog alters dorsal-ventral patterning of somites. <i>Cell</i> 79, 1165-1173 (December 1994).	
	EA	Johnson, R. L. et al. Mechanism of limb patterning. <i>Curr. Opin. Genet. Dev.</i> 4, 535-542 (August 1994).	
	EB	Johnson, R. L. et al. Patched overexpression alters wing disc size and pattern: transcriptional and post-transcriptional effects on hedgehog targets. <i>Devel.</i> 121, 4237-4245 (December 1995).	
	EC	Johnson, R. L. et al. Sonic hedgehog: a key mediator of anterior-posterior patterning of the limb and dorso-ventral patterning of axial embryonic structures. <i>Biochem. Soc. Trans.</i> 22, 569-574 (August 1994).	
	ED	Jones, M. et al. Involvement of bone morphogenetic protein-4 (BMP-4) and Vgr-1 in morphogenesis and neurogenesis in the mouse. <i>Devel.</i> 111, 531-542 (1991).	
	EE	Kalderon, D. Morphogenetic signaling. Responses to hedgehog. <i>Curr. Biol.</i> 5, 580-582 (June 1995).	
	EF	Koonin, E. A protein splice-junction motif in hedgehog family proteins. <i>Trends Biochem. Sci.</i> 20, 141-142 (April 1995).	
	EG	Kornblihtt, A. R. et al. Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene. <i>EMBO J.</i> 4, 1755-1759 (1985).	
	EH	Kornfeld, R. & Kornfeld, S. Assembly of asparagine-linked oligosaccharides. <i>Ann. Rev. Biochem.</i> 54, 631-664 (1985).	
	EI	Krauss, S. et al. Expression of the zebrafish paired box gene pax[zf-b] during early neurogenesis. <i>Devel.</i> 113, 1193-1206 (1991).	
	EJ	Krauss, S. et al. A functionally conserved homolog of the Drosophila Segment polarity gene hh is expressed in tissues with polarizing activity in zebrafish embryos. <i>Cell</i> 75, 1431-1444 (1993).	
	EK	Lai, C. et al. Patterning of the neural ectoderm of <i>Xenopus laevis</i> by the amino-terminal product of hedgehog autoproteolytic cleavage. <i>Devel.</i> 121, 2349-2359 (1995).	
EL	Laufer, E. et al. Sonic hedgehog and Fgf-4 act through signaling cascade and feedback loop to integrate growth and patterning of hedgehog. <i>Cell</i> 71, 33-50 (1992).		
EM	Lee, J. J. et al. Secretion and localized transcription suggest a role in positional signaling for products of the segmentation gene hedgehog. <i>Cell</i> 71, 33-50 (1992).		

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	EN	Lee, J. J. et al. Autoproteolysis in hedgehog protein biogenesis. <i>Science</i> 266, 1528-1537 (December 1994).	
		Lee, S. J. Expression of growth/differentiation factor1 in the nervous system: Conservation of a bicistronic structure. <i>PNAS</i> 88, 4250-4254.	
		Levin, M. et al. A molecular pathway determining left-right asymmetry in chick embryogenesis. <i>Cell</i> 82, 803-814 (8 September 1995).	
	EQ	Li, W. et al. Function of protein kinase A in hedgehog signal transduction and drosophila imaginal disc development. <i>Cell</i> 80, 553-562 (February 1995).	
	ER	Lopez-Martinez, A. et al. Limb-patterning activity and restricted posterior localization of the amino-terminal product of sonic hedgehog cleavage. <i>Curr. Biol.</i> 5, 791-796 (July 1995).	
	ES	Lumsden, A. & Graham, A. Neural patterning: A forward role for hedgehog. <i>Curr. Biol.</i> 5, 1347-1350 (December 1995).	
	ET	Ma, C. et al. Molecular cloning and characterization of rKlk10, a cDNA encoding T-kininogenase from rat submandibular gland and kidney. <i>Biochem.</i> 31, 10922-10928 (1992).	
	EU	Maccabe, J. A. & Parker, B. W. The target tissue of limb-bud polarizing activity in the induction of supernumerary structures. <i>J. Embryol. Exp. Morph.</i> 53, 67-73 (1979).	
	EV	Maiese, K. et al. Protein kinases modulate the sensitivity of hippocampal neurons to nitric oxide toxicity and anoxia. <i>J. Neurosci. Res.</i> 36, 77-87 (1993).	
	EW	Marigo, V. et al. Biochemical evidence that patched is the hedgehog receptor. <i>Nature</i> 384, 176-179 (1996).	
	EX	Marti, E. et al. Distribution of Sonic hedgehog peptides in the developing chick and mouse embryo. <i>Devel.</i> 121, 2537-2547 (August 1995).	
	EY	Marti, E. et al. Requirement of 19K form of Sonic hedgehog for induction of distinct ventral cell types in CNS explants. <i>Nature</i> 375, 322-325 (May 1995).	
	EZ	Mavillio, F. et al. Activation of four homeobox gene clusters in human embryonal carcinoma cells induced to differentiate by retinoic acid. <i>Differentiation</i> 37, 73-79 (1988).	
	FA	McGinnis, W. & Krumlauf, R. Homeobox genes and axial patterning. <i>Cell</i> 68, 283-302 (1992).	
	FB	Mohler, J. Requirements for hedgehog, a segmental polarity gene, in patterning larval and adult cuticle of drosophila. <i>Genetics</i> 120, 1061-1072 (1988).	
FC	Mohler, J. & Vani, K. Molecular organization and embryonic expression of the hedgehog gene involved in cell-cell communication in segmental patterning of drosophila. <i>Devel.</i> 115, 957-971 (1992).		
FD	Morgan, B. A. et al. Targeted misexpression of Hox-4.6 in the avian limb bud causes apparent homeotic transformations. <i>Nature</i> 358, 236-239 (1992).		

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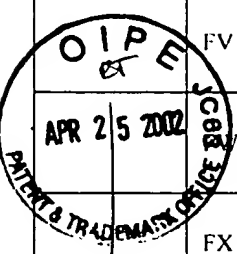
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	FE	Nakano, Y. et al. A protein with several possible membrane-spanning domains encoded by the Drosophila segment polarity gene patched. <i>Nature</i> 341, 508-513 (1989).	
	FF	Ngo, J. et al. Computational Complexity Protein. Merz & LeGrand, eds. @ Birkhauser Boston (1994).	
	FG	Niswander, L. & Martin, G. R. FGF-4 and BMP-2 have opposite effects on limb growth. <i>Nature</i> 361, 68-71 (1993).	
	FH	Niswander, L. et al. A positive feedback loop coordinates growth and patterning in the vertebrate limb. <i>Nature</i> 371, 609-612 (13 October 1994).	
	FI	Nohno, T. et al. Involvement of the Chox-4 Chicken Homeobox Genes in Determination of Anteroposterior Axial Polarity During Limb Development. <i>Cell</i> 64, 1197-1205 (22 March 1991).	
	FJ	Nohno, T. et al. Involvement of the Sonic hedgehog gene in chick feather formation. <i>Biochem. Biophys. Res. Comm.</i> 206, 33-39 (January 1995).	
	FK	O'Farrell, P. H. Unanimity waits in the wings. <i>Nature</i> 368, 188-189 (1994).	
	FL	Ontogeny's "****hedgehog****" for degenerative diseases (1995) <i>Script</i> 2032, p26	
	FM	Parisi, Michael J., et al., The Role of the Hedgehog/Patched Signaling Pathway in Epithelial Stem Cell Proliferation: From Fly to Human, (1998) <i>Cell Research</i> 8, 15-21	
	FN	Parr, B. A. et al. Mouse Wnt genes exhibit discrete domains of expression in the early embryonic CNS and limb buds. <i>Devel.</i> 119, 247-261 (1993).	
	FO	Patel, N. H. et al. The role of segment polarity genes during Drosophila neurogenesis. <i>Genes & Devel.</i> 3, 890-904 (1989).	
	FP	Peifer, M. The two faces of hedgehog. <i>Science</i> 266, 1492-1493 (December 1994).	
	FQ	Perrimon, N. Hedgehog and beyond. <i>Cell</i> 80, 517-520 (24 February 1995).	
	FR	Perrimon, N. et al. Generating lineage-specific markers to study Drosophila development. <i>Develop. Genet.</i> 12, 238-252 (1991).	
	FS	Pham, A. et al. The Suppressor of fused gene encodes a novel PEST protein involved in Drosophila segment polarity establishment. <i>Genetics</i> 140, 587-598 (June 1995).	
FT	Phillis, J. W. & O'Regan, M. H. Mechanisms of glutamate and aspartate release in the ischemic rat cerebral cortex. <i>Brain Res.</i> 730, 150-164 (1996).		
FU	Placzek, M. et al. Induction of floor plate differentiation by contact-dependent, homeogenetic signals. <i>Devel.</i> 117, 205-218 (1993).		

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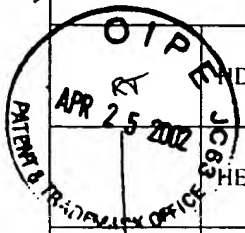
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	FV	Placzek, M. et al. Orientation of Commissural Axons in vitro in response to a floor plate-derived chemoattractant. <i>Devel.</i> 110, 19-30 (1990).	
		Pollock, R. A. et al. Altering the boundaries of Hox3.1 expression: Evidence for antipodal gene regulation. <i>Cell</i> 71, 911-923 (1992).	
	FX	Porter, J. et al. The product of hedgehog autoproteolytic cleavage active in local and long-range signaling. <i>Nature</i> 374, 363-366 (23 March 1995).	
	FY	Reeck, et al. Homology in proteins and nucleic acids: A terminology muddle and a way out of it. <i>Cell</i> 50, 667 (28 August 1987).	
	FZ	Rennie, J. Super sonic. <i>Sci. Amer.</i> P20 (April 1994).	
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		Applicant Wang, Elizabeth	
		Filing Date April 5, 2001	Group Art Unit 1653
GM	Shi, Yun-Bo. Cell-Cell and Cell-ECM Interactions in Epithelial Apoptosis and Cell Renewal During Frog Intestinal Development, (1995) Cell Biochem. and Biophys. 179-202		
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GS	Tabin, C. J. Retinoids, homeoboxes, and growth factors: Toward molecular models for limb development. <i>Cell</i> 66, 199-217 (26 July 1991).		
GT	Tanabe, Y. et al. Induction of motor neurons by sonic hedgehog is independent of floor plate differentiation. <i>Curr. Biol.</i> 5, 651-658 (June 1995).		
GU	Tanaka, E. & Gann, A. Limb development: The budding role of FGF. <i>Curr. Biol.</i> 5, 594-597 (June 1995).		
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		Vogel, A. & Tickle C. FGF-4 maintains polarizing activity of posterior limb bud cells in vivo and in vitro. <i>Devel.</i> 119, 199-206 (1993).			
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EXAMINER <i>R. Teller</i>			DATE CONSIDERED <i>2/14/03</i>		
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